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08/881,509	06/24/97	SCHENDEL	D P564-7015

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EXAMINER
DECLoux, A

ART UNIT	PAPER NUMBER
1644	19

DATE MAILED: 06/30/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.

08/881,509

Applicant(s)

Schendel

Examiner

DeCloux, Amy

Group Art Unit

1644



☒ Responsive to communication(s) filed on received April 19, 2000

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claim

- ☒ Claim(s) 1-44 is/are pending in the application.
- Of the above, claim(s) 8-25 and 27-44 is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 1-7 and 26 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

- ☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☒ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☒ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- ☒ Notice of References Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- ☐ Interview Summary, PTO-413
- ☒ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Serial No. 08/881,509  
Art Unit 1644

### DETAILED ACTION

1. Applicant's election with traverse of Group I in Paper No. 17, received 4-19-00, is acknowledged. The traversal is on the ground(s) that Group VI should be examined with Group I because it would not be an undue burden on the examiner to include a method using the nucleic acid and composition in the search of the nucleic acid and composition. This is not found persuasive because of the reasons of record and because a search of the methods of using the claimed product would not be co-extensive with a search of the claimed product, and as evidenced by their distinct classification in the art. Therefore, an examination and search of both groups in a single application would constitute a serious undue burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-25, and 27-44 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claim 26 is only being examined for the nucleic acid embodiment, since it was listed in the restriction as being in Groups I, II and III.

2. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

3. Claim 26 is objected to for being dependent upon claims 8, 9, 18-24, which was not elected.

4. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title".

5. Claims 1-4 and 6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. "Nucleic acid which codes for the alpha chain of a human T cell receptor", specifically V $\alpha$ 20 and J $\alpha$ 22, as recited in claims 1-4, would read on an entire chromosome in T cells that had undergone a VJ recombination as evidenced by their expression of T lymphocytes expressing a TCR comprising a V $\alpha$ 20 and J $\alpha$ 22, such as the TILs isolated from human Renal Cell Carcinoma CTLs taught by Jantzer et al (1998) (Cancer Res. 58:3078-3086), and thus would be compositions of nature and constitutes non-statutory subject matter. Claim 6 recites a cell that contains the DNA of claims 1-4, which may be present in a patient

with kidney carcinoma as disclosed in the instant specification, and therefore would read upon a cell of an intact organism, which is a naturally-occurring product of nature and thus constitutes non-statutory subject matter.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7A) Claims 1-7 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid which codes for an alpha chain of the human T cell receptor comprising SEQ ID NO:23 where  $X_1...X_n$  is one of the amino acid sequences recited in claims 3 and 4 of the instant application, a Fab, a single chain antibody, or soluble TCR fragments thereof, and a composition thereof, does not reasonably provide enablement for the broader recitation of any "functional derivative or any fragment thereof" or composition thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides the nucleic acid that encodes for a human T cell receptor comprising SEQ ID NO:23, where  $X_1...X_n$  is one of the amino acid sequences recited in claims 3 and 4 of the instant application, a Fab, a single chain antibody, or a soluble TCR fragment, or composition thereof, the specification fails to provide sufficient guidance in determining if a nucleic acid that encodes any derivative or any fragment of the recited alpha chain will encode an alpha chain of a T cell receptor (TCR) with the desired specificity. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of nucleic acids which code for a "functional derivative or fragment thereof" where the expectation of retaining similar encoding function is unpredictable based on the instant disclosure. Detailed information regarding the structural and functional requirements of the CDR3 region of an alpha TCR specific for kidney carcinoma, other than the CDR3 sequences recited in claims 3 and 4, is lacking. Also, recognition of a T cell epitope depends on the interaction of

CDR3 with the MHC-peptide complex. Therefore, predicting that any functional derivative or any fragment thereof that would maintain the desired specificity is well outside the realm of routine experimentation; thus a skilled artisan would require guidance, such as information regarding the size and sequence of derivatives and fragments which preserve the TCR specificity, in order to make and use polynucleotides, probes, vectors, host cells and recombinant methods in a manner reasonably commensurate with the scope of the claims. Thus, it would require undue experimentation of one skilled in the art to practice the claimed invention. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

7B) Claims 1-2, 5-7 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid which codes for an alpha chain of the human T cell receptor comprising SEQ ID NO:23, where  $X_1...X_n$  is one of the amino acid sequences recited in claims 3 and 4 of the instant application, a Fab, a single chain antibody, or soluble TCR fragments thereof, and a composition thereof, does not reasonably provide enablement for the broader recitation where x is any amino acid as recited in claim 2, or for a nucleic acid which codes for any TCR alpha chain comprising a CDR3 region formed from a combination of a  $V\alpha 20$  and  $J\alpha 22$  gene segment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Besides the nucleic acid that encodes for a human T cell receptor comprising SEQ ID NO:23, where  $X_1...X_n$  is one of the amino acid sequences recited in claims 3 and 4 of the instant application, a Fab, a single chain antibody, or a soluble TCR fragment, or composition thereof, the specification fails to provide guidance as to how to determine if a nucleic acid that comprises  $X_1...X_n$  amino acid residues of any type, or that comprises any  $V\alpha 20$  and  $J\alpha 22$  combination, will convey the desired specificity on the CDR3 of the alpha chain.

As discussed above, detailed information regarding the structural and functional requirements of the CDR3 region of an alpha TCR specific for kidney carcinoma, other than the recited CDR3 sequences in Claims 3 and 4, is lacking. Since recognition of the MHC-peptide complex depends in part on its interaction with CDR3, and since there is insufficient guidance as to which, if any, amino acid substitutions for  $X_1...X_n$  in the CDR3 (other than

those recited in Claims 3 and 4), or which combination of V $\alpha$ 20 and J $\alpha$ 22 gene segments in view of junctional diversity generated during said combination, would confer the desired specificity of the TCR, predicting which amino acids to insert in the CDR3 of SEQ ID NO:23, or which combination of V $\alpha$ 20 and J $\alpha$ 22 gene segments that would maintain the desired specificity is well outside the realm of routine experimentation; thus a skilled artisan would require guidance, such as information regarding the number and sequence of the amino acids which preserve the desired TCR specificity, in order to make and use polynucleotides, probes, vectors, host cells and recombinant methods in a manner reasonably commensurate with the scope of the claims. Thus, it would require undue experimentation of one skilled in the art to practice the claimed invention. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

8. Claims 2-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide enablement for a nucleic acid which comprises a nucleotide sequence that encodes a polypeptide with at least 80% identity to SEQ ID NO:23. Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar functions and properties of the encoded product requires a knowledge of, and guidance with regard to which amino acids encoded by the nucleotide sequence, if any, are tolerant of modification and which are conserved or less tolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. However, the problem of predicting functional aspects of the product from mere sequence data of a single nucleic acid sequence and what changes can be tolerated is complex and well outside the realm of routine experimentation. Without such guidance, a nucleic acid encoding an alpha chain of a human TCR comprising a CDR3 that is 80% identical to that

of SEQ ID NO:23, and still possessing the desired specificity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. *In re Fisher*, 1666 USPQ 19 24 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Without such guidance, the nucleotide substitutions which can be made and used to encode the CDR3 with the desired specificity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly extensive and undue. See *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). Therefore, there is no evidence of record to show that one skilled in the art would be able to practice the invention as claimed without an undue amount of experimentation.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

10. Claims 2-7 and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

A) Claims 2-7 and 26 are indefinite in the recitation of the phrase "equivalent recognition specificity" because it is not clear what said phrase refers to; does applicant mean an equivalent recognition specificity as that of an amino acid sequence comprising SEQ ID NO:23? OK

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the

Serial No. 08/881,509  
Art Unit 1644

2

PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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June 30, 2000

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ART UNIT 182/1644